Application No.: 10/623076 Docket No.: BPI-189

In the claims:

Please amend claims 35-37 as follows:

1. **(Original)** A method of treating idiopathic interstitial lung disease or a chronic obstructive airway disorder in a subject comprising administering to the subject a therapeutically effective amount of a neutralizing, high affinity TNFα antibody, such that said disorder is treated.

2. **(Original)** The method of claim 1, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNFα with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less.

3. **(Original)** The method of claim 1, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof with the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

4. **(Original)** The method of claim 1, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO:1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

5. **(Original)** The method of any one of claims 1, 2, 3, or 4, wherein the antibody is D2E7.

6. **(Original)** The method of any one of claims 1, 2, 3, or 4, wherein the idiopathic interstitial lung disease is idiopathic pulmonary fibrosis.

7. **(Original)** The method of any one of claims 1, 2, 3, or 4, wherein the chronic obstructive airway disorder is asthma or chronic obstructive pulmonary disease (COPD).

8. **(Original)** A method of treating a subject suffering from an idiopathic interstitial lung disease comprising administering a therapeutically effective amount of a TNFα antibody, or an antigen-binding fragment thereof, to the subject, wherein the antibody dissociates from human TNFα with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less, such that the idiopathic interstitial lung disease is treated.

9. **(Original)** A method of treating a subject suffering from an idiopathic interstitial lung disease comprising administering a therapeutically effective amount a TNFα antibody, or an antigen-binding fragment thereof, with the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12, such that the idiopathic interstitial lung disease is treated.

10. **(Original)** A method of treating a subject suffering from an idiopathic interstitial lung disease comprising administering a therapeutically effective amount a TNFα antibody, or an antigen-binding fragment thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2, such that the idiopathic interstitial lung disease is treated.

11. **(Original)** A method of treating a subject suffering from a chronic obstructive airway disorder comprising administering a therapeutically effective amount of a TNFα antibody, or an antigen-binding fragment thereof, to the subject, wherein the antibody dissociates from human TNFα with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less, such that the chronic obstructive airway disorder is treated.

12. **(Original)** A method of treating a subject suffering from a chronic obstructive airway disorder comprising administering a therapeutically effective amount a TNFα antibody, or an antigen-binding fragment thereof, with the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12 such that the chronic obstructive airway disorder is treated.

13. **(Original)** A method of treating a subject suffering from a chronic obstructive airway disorder comprising administering a therapeutically effective amount a TNFα antibody, or an antigen-binding fragment thereof, with a light chain variable region (LCVR) comprising the

amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2 such that the chronic obstructive airway disorder is treated.

14. **(Original)** The method of any one of claims 8 to 13, wherein the antibody, or antigen-binding fragment thereof, is D2E7.

15. **(Original)** The method of any one of claims 8, 9, or 10, wherein the idiopathic interstitial lung disease is idiopathic pulmonary fibrosis.

16. **(Original)** The method of any one of claims 11, 12, or 13, wherein the chronic obstructive airway disorder is asthma or COPD.

17. **(Original)** A method of treating a subject suffering from a pulmonary disorder selected from the group consisting of asthma, chronic obstructive pulmonary disease, and idiopathic pulmonary fibrosis comprising administering a therapeutically effective amount of a TNFα antibody, or an antigen-binding fragment thereof, to the subject, wherein the antibody dissociates from human TNFα with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less, such that said pulmonary disorder is treated.

18. **(Original)** A method of treating a subject suffering from a pulmonary disorder selected from the group consisting of asthma, COPD, and idiopathic pulmonary fibrosis comprising administering a therapeutically effective amount a TNFα antibody, or an antigen-binding fragment thereof, with the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12, such that said pulmonary disorder is treated.

19. **(Original)** A method of treating a subject suffering from a pulmonary disorder selected from the group consisting of asthma, COPD, and idiopathic pulmonary fibrosis comprising administering a therapeutically effective amount a TNFα antibody, or an antigen-binding fragment thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2, such that said pulmonary disorder is treated.

20. **(Original)** The method of any one of claims 17, 18, or 19, wherein the TNFα antibody, or antigen binding fragment thereof, is D2E7.

21. **(Original)** The method of any one of claims 17, 18, or 19, wherein the TNFα antibody is administered with at least one additional therapeutic agent.

22. **(Original)** A method for inhibiting human TNFα activity in a human subject suffering from an idiopathic interstitial lung disease comprising administering a therapeutically effective amount of a TNFα antibody, or an antigen-binding fragment thereof, to the subject, wherein the antibody dissociates from human TNFα with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less.

23. **(Original)** The method of claim 22, wherein the idiopathic interstitial lung disease is idiopathic pulmonary fibrosis.

24. **(Original)** A method for inhibiting human TNFα activity in a human subject suffering from a chronic obstructive airway disorder comprising administering a therapeutically

effective amount of a TNFα antibody, or an antigen-binding fragment thereof, to the subject, wherein the antibody dissociates from human TNFα with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less.

25. **(Original)** The method of claim 24, wherein the chronic obstructive airway disorder is asthma or COPD.

26. **(Original)** The method of any one of claims 22 to 25, wherein the TNFα antibody, or antigen-binding fragment thereof, is D2E7.

27. **(Original)** A method for inhibiting human TNFα activity in a human subject suffering from a pulmonary disorder selected from the group consisting of asthma, COPD, and idiopathic pulmonary fibrosis, comprising administering a therapeutically effective amount of a TNFα antibody, or an antigen-binding fragment thereof, to the subject, wherein the antibody dissociates from human TNFα with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less.

28. **(Original)** The method of claim 27, wherein the antibody, or antigen binding fragment thereof, is D2E7.

29. **(Original)** A method of treating a subject suffering from an idiopathic interstitial lung disease comprising administering a therapeutically effective amount of D2E7, or an antigen-binding fragment thereof, to the subject, such that the disease is treated.

30. **(Original)** The method of claim 29, wherein the idiopathic interstitial lung disease is idiopathic pulmonary fibrosis.

31. **(Original)** A method of treating a subject suffering from a chronic obstructive airway disorder comprising administering a therapeutically effective amount of D2E7, or an antigen-binding fragment thereof, to the subject, such that the disorder is treated.

32. **(Original)** The method of claim 31, wherein the chronic obstructive airway disorder is asthma or COPD.

33. **(Original)** A method of treating a subject suffering from a pulmonary disorder selected from the group consisting of asthma, idiopathic pulmonary fibrosis, and COPD comprising administering a therapeutically effective amount of D2E7, or an antigen-binding fragment thereof, to the subject, such that the disorder is treated.

34. **(Original)** A method of treating a subject suffering from asthma, idiopathic pulmonary fibrosis, and COPD comprising administering a therapeutically effective amount of D2E7, or an antigen-binding fragment thereof, and at least one additional therapeutic agent to the subject, such that the disorder is treated.

35. **(Currently amended)** A kit comprising:

a) a pharmaceutical composition comprising a TNFα antibody, or an antigen binding portion thereof, and a pharmaceutically acceptable carrier, wherein the antibody dissociates from human TNFα with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less; and

b) instructions for administering to a subject the TNFα antibody pharmaceutical composition for treating a subject who is suffering from asthma.

36. **(Currently amended)** A kit comprising:

a) a pharmaceutical composition comprising a TNFα antibody, or an antigen binding portion thereof, and a pharmaceutically acceptable carrier wherein the antibody dissociates from human TNFα with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both

determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less; and

b) instructions for administering to a subject the TNFα antibody pharmaceutical composition for treating a subject who is suffering from COPD.

37. **(Currently amended)** A kit comprising:

a) a pharmaceutical composition comprising a TNFα antibody, or an antigen binding portion thereof, and a pharmaceutically acceptable carrier, wherein the antibody dissociates from human TNFα with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less; and

b) instructions for administering to a subject the TNFα antibody pharmaceutical composition for treating a subject who is suffering from idiopathic pulmonary fibrosis.

38. **(Currently amended)** A kit according to any one of claims 35, 36, or 37, wherein the TNFα antibody, or an antigen binding portion thereof, is D2E7.